How does an explicit potential gradient influence a channel? Initial steps for the Kv1.2 channel in an all-atom simulation

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WHY STUDY POTASSIUM CHANNELS?

Voltage-dependent potassium channels conduct potassium ions across the cell membrane. The voltage sensor domain moves in response to differences in electrical potential across the membrane effecting a transition between the open and closed states of the channel.
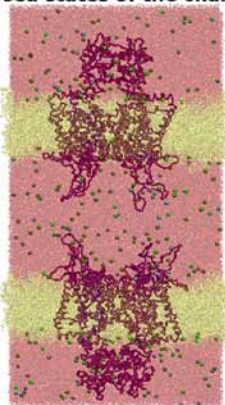
The main focus of our project is to investigate the mammalian potassium channel, Kv1.2, and understand how the channel fluctuates in the context of an electrified interface.

SIMULATION METHOD

- Mammalian Kv1.2 channel → residues 32 through 421 of the entire channel

- System built using Charmm version c32b1
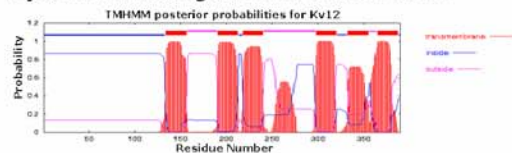
- Total of 5 systems each with varying transmembrane potentials:
  - 2 hyperdepolarized (negative & negative(2)), 1 neutral, and 2 hyerpolarized (positive & positive(2))
  - Each system contains 685,456 atoms

- Simulation run using LAMMPS

- Simulation run with an NPT ensemble for 10 ns and an equilibration time of 1 ns

POTENTIAL PROFILE RESULTS
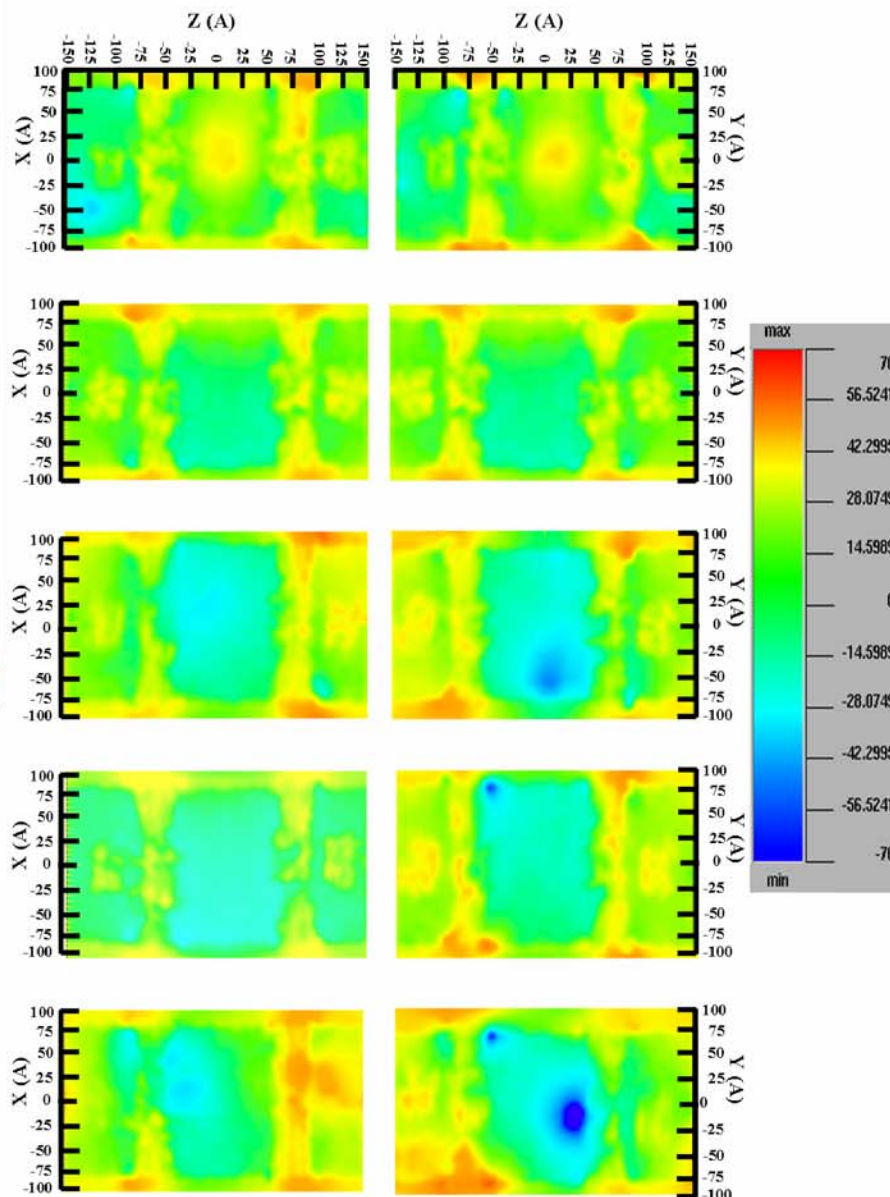
ANGLE TIME EVOLUTION RESULTS
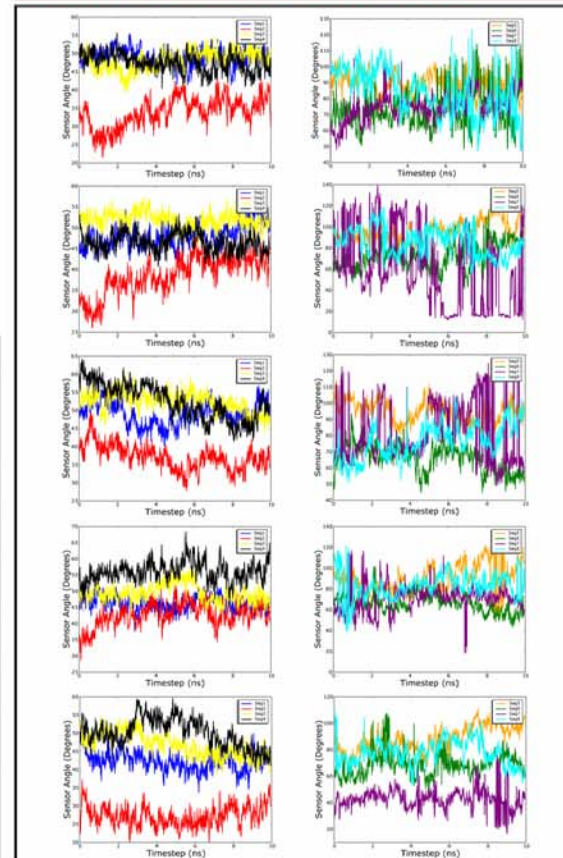
SUMMARY

- Time average RMS fluctuations for the helical regions show stability of all systems.

- The time evolution results show that S4 region exhibits two-state-like transitions for its orientation relative to the bilayer for some simulations.

- Potential profiles show differences between all systems.

ACKNOWLEDGEMENTS